Cocaine abuse and dependence linked to genetic risk factors among female twins

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Question

How much influence do genetic and environmental risk factors have on lifetime cocaine use, abuse, and dependence in women?

Design

A population-based cohort study using data from a twin registry

Setting

Virginia

Participants

A total of 1937 out of 2288 eligible white women (mean age 37 years) were interviewed. Participants were members of female-female pairs listed in the Virginia Twin Registry. Data for 1934 women were included in the analysis; both twins were included for 485 monozygotic (MZ) pairs and 335 (DZ) dizygotic pairs.

Assessment of risk factors

Zygosity was determined blindly by standard questions, photographs, and DNA when necessary. Telephone interviewers, who were blind to information about the co-twin, asked questions about childhood (how often the twins shared the same room at home, were in the same class at school, and were dressed alike); adolescence (how often they had the same friends, were in the same social group, and went out together to films and dances); and adulthood (how much contact they had had in the previous year). These data were used to assess the similarity of environments for each pair of twins.

Main outcome measures

Lifetime cocaine use, abuse, and dependence were assessed by an adapted Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 3rd ed., revised (DSM-III-R), patient version interview. Cocaine abuse and dependence were diagnosed by using DSM-IV criteria.

Main results

MZ and DZ twins whose co-twins had used cocaine were more likely to use cocaine than those whose co-twins had not used cocaine (odds ratio [OR] 14.2, 95% confidence interval [CI] 8.7 to 23.2 for MZ twins; OR 6.7, 95% CI 3.9 to 11.7 for DZ twins). MZ twins were also more likely to abuse or be dependent on cocaine if their co-twins had abused or been dependent on cocaine (OR 40.8, 95% CI 16.3 to 102.4 for abuse; OR 27.6, 95% CI 9.4 to 81.5 for dependence). For DZ twins, cocaine abuse and dependence did not have statistically significant associations with cocaine abuse (OR 2.70, 95% CI 0.6 to 13.1) or dependence in the co-twin (OR not estimated because no DZ twins were concordant). Tetrachoric correlations were high for cocaine use, abuse, and dependence in MZ twins ($r = 0.73$, $r = 0.80$, and $r = 0.68$, respectively). In DZ twins, the correlation was greater for cocaine use ($r = 0.54$) than for cocaine abuse ($r = 0.18$) or dependence ($r = 0.08$). Models developed to fit data showed cocaine abuse and dependence were influenced mainly by genetic risk factors, which explained 79% of the variance for abuse and 65% of the variance for dependence. For cocaine use, 39% of the variance was explained by genetic and 35% by environmental risk factors.

Conclusion

Lifetime cocaine abuse and dependence in women were mainly influenced by genetic risk factors. Lifetime cocaine use in women was influenced partly by genetic and partly by environmental risk factors.

COMMENTARY

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Family, twin, and adoption studies are the cornerstone of genetic epidemiology. In psychiatry, these paradigms enhance our understanding of putative causal mechanisms, although direct evidence for genetic and environmental determinants remains to be elucidated for the major psychiatric disorders. Many practitioners are optimistic about the recent advances in molecular biology, and they believe that the identification of genetic factors is within our reach for some of these disorders. Evidence from family, twin, and adoption studies provides essential stepping stones for the identification of genetic factors that can be investigated further in linkage and segregation studies.

A combination of these approaches has uncovered compelling evidence for the role of genetic factors in substance abuse (as reviewed in the study by Kendler and Prescott). This study adds an additional piece to this complex puzzle and is a major contribution to the literature because it is the first reported twin study of cocaine use and abuse in women.

The strengths of this study lie in its excellent methodology, including the community-based twin sample, which enhances the generalizability of the findings; the blinding of the interviewers; the use of standardized diagnostic criteria; the examination of multiple sources of potential bias that might attenuate or diminish effect sizes; and the statistical approach used to show twin resemblance for liability to cocaine use and abuse.

The inherent weakness of this study, as reported by the authors, is the small number of twins who had abuse or dependence problems. Although the proportions of cocaine use, abuse, and dependence are similar to what is reported in the National Comorbidity Survey, the small number of affected twins makes it difficult to estimate the magnitude of the genetic effect. It is clear that these findings need to be replicated in a larger sample of female twins. It would be of additional clinical interest to conduct a longitudinal study to determine whether the course and outcome differ in men and women.

The clinical implications of these findings for practice are subtle yet important. They include the need to establish a family history of substance use and abuse and the need to gather information during clinical interviews to distinguish between the use and abuse of substances. These 2 sources of information may be particularly important if future studies show that the magnitude of the genetic effect is associated with differential responses to treatment.